REMARKS

This submission is in response to the Office Action dated June 18, 2001. A petition for one month extension of time and the appropriate fees are submitted herewith. No other fees are believed to be due. If it is determined that any additional fees are due, the Assistant Commissioner is authorized to charge or credit our Deposit Account No. 50-0552.

Reconsideration and withdrawal of the rejection of this application in view of the above amendments and the remarks set forth below are respectfully requested.

Attached hereto is a marked up version of the changes made to the claims by the current amendment. The attached pages are entitled "Version of claim amendments with markings to show changes made."

An early and favorable action on the merits is earnestly solicited.

Status of the Claims

Claims 1, 3-6, 14 and 16-22 are pending in the application. Claims 1, 4, 5, 6, 14, 16, 18 and 20 have been amended. Support for these amendments is found in the specification as more specifically discussed below. No new matter has been added by way of those amendments.

Objections to Claims

Claim 14 has been objected to under 37 C.F.R. §1.75(c) as being in improper multiple dependent form. Claim 14 has been amended by canceling "and" and substituting therefore --or--. It is now believed that the Examiner's objection has been obviated.

Rejections Under 35 U.S.C. §112, First and Second Paragraphs

Claims 1, 3-6, 14, 16-22 have been rejected under 35 U.S.C. §112 first and/or second paragraphs as more specifically discussed on pages 3 and 4 of the Office Action. In response to these rejections Applicants have amended the claims as further discussed below.

Applicants' representative thanks Examiner Saunders for helpful suggestions and other courtesies extended during an informal telephone interview conducted on September 25, 2001 with the undersigned.

Claim 6 has been amended by deleting the term "greatly". As now amended claim 6 recites a heparin binding protein wherein the addition of the sugar chain will not change the tertiary structure "sufficiently to cause the protein to incur a loss of activity" which is language that can be understood by one skilled in the art. Support for this amendment is also provided at page 10, lines 24 et seq. of the specification and by the originally filed claim 6.

With respect to the new matter rejections, applicants have amended all independent claims to recite that "the residual activity of the heparin-binding peptide is increased for the intended medical use by adding the covalently bonded sugar chain". Support for this amendment is provided in the specification at page 7, line 6 and also on page 16, line 2 et seq. Moreover, the amended language includes terminology suggested by the Examiner in the first full paragraph on page 4 of the Office Action.

Claim 1 has been amended to delete reference to "at least one" and substitute therefor --a--. With respect to support for the use of "at least one" in claims 16 and 20 and "plurality of covalently bonded sugar chains" recited in claim 19, Applicants submit that many of the amino acid sequences recited in the specification contain amino acid residues as glycosylation sites that could and do become glycosylated. It is well established that glycosylation occurs at serine/threonine residue sites. For example, several serine residue sites capable of glycosylation are shown in red in the asterisked portions of SEQ ID NOS. 17, 19, 1, 21 and 23. See attached Exhibit A.

The serine residue sites of the heparin-binding protein and their vicinity can be considered to be similar to portions of the structure of naturally occurring human glycoprotein syndecan-4 shown at the top of Exhibit A. Shworak et al. in J. Biol. Chem., 269, 21204-21214 (1994), analyzed the syndecan-4 and reported that a few of serine residues, colored in red in Exhibit A were modified as a whole with a plurality of glycosaminoglycan sugar chains at those serine sites. Applicants submit that by analogy*, there are several serine sites as shown for SEQ ID Nos. 17, 19, 1, 21 and 23 at which glycosylation of the heparin-binding protein occurs.

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* See explanation by the same inventorship in Nature Biotechnology, 18, 641-444, (2000) at 641, in the right column.

Copies of both publications by Shworak et al. and Yoneda et al. are attached as Exhibits B and C, respectively.

Furthermore, Applicants have conducted an experiment in which the protein of SEQ ID NO. 1 was modified by substituting one or two serine residues (out of the three modifiable serines at 39, 61 and 63) with non-modifiable amino acids. The molecular weight of total sugars thereof was smaller than that of the original protein, but not zero. This also supports the fact that the modification of the heparin-binding protein of the invention can be accomplished with a plurality of sugar chains.

Claim 20 has been amended to recite "containing a" peptide "sequence". Support for this amendment is found at page 7, line 6 of the specification. Support for the term "improved heparin-binding protein" used in claims 18 and 20 is provided at page 3, line 18 of the specification. Moreover, the allegedly indefinite language "can be" was substituted with --is-- as requested by the Examiner. It is, therefore, submitted that as now amended the rejections of the claims under 35 U.S.C. §112, first and second paragraph have been obviated and the withdrawal of such rejections is earnestly solicited.

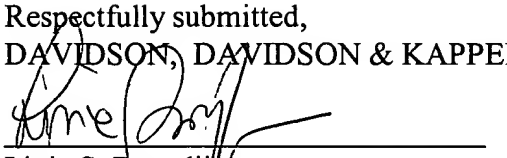
Applicants gratefully acknowledged that the amendments filed on March 8, 2001 and April 5, 2001 have overcome the previously stated rejection of claims 1-3, 6 and 14 under 35 U.S.C. §102(b) as being anticipated by U.S. Patent No. 5,360,896 to Senoo et al.

In view of the amendments and remarks set forth above, it is respectfully submitted that the present application is in condition for allowance, which allowance is earnestly solicited.

Additionally, if the Examiner is of the view that there are issues still pending which present an impediment to allowance, it is respectfully requested that the undersigned be contacted

by telephone to conduct a telephone interview prior to issuance of the next Official Action in order to resolve such outstanding issues.

Respectfully submitted,
DAVIDSON, DAVIDSON & KAPPEL, LLC



Livia S. Boyadjian
Reg. No. 34,781
Clifford M. Davidson
Reg. No. 32,728

Davidson, Davidson & Kappel, LLC
485 Seventh Avenue, 14th Floor
New York, New York 10018
(212) 736-1940

VERSION OF CLAIM AMENDMENTS
WITH MARKINGS TO SHOW CHANGES MADE

1. (Twice Amended) A heparin-binding protein comprising [at least one] a covalently bonded sugar chain, [wherein the at least one] said sugar chain selected from the group consisting of a sulfated polysaccharide, a glycosaminoglycan, an O-linked sugar chain and combinations thereof, wherein the residual activity of the heparin-binding peptide for the intended medical use is increased by adding the covalently bonded sugar chain.

4. (Twice Amended) The heparin-binding protein of claim 1, wherein the [at least one] sugar chain is covalently bonded through a peptide to which the [at least one] sugar chain can be added.

5. (Thrice Amended) The heparin binding protein of claim 4, wherein the heparin-binding protein comprising the [at least one] covalently bonded sugar chain comprises:

(a) a protein consisting of the amino acid sequence of SEQ ID NO: 1, 17, 19, 21, 23, or 29; or

(b) a protein which consists of the amino acid sequence of SEQ ID NO: 1, 17, 19, 21, 23, or 29 having a deletion, substitution, addition or modification of at least one amino acid, wherein the heparin-binding protein comprising [at least one] the covalently bonded sugar chain has FGF activity and wherein the peptide to which the sugar chain can be added comprises a proteoglycan core protein or a part thereof.

6. (Twice Amended) The heparin binding protein of claim 1, wherein the [at least one] sugar chain is bonded to the heparin-binding protein at a site forming a turn in the secondary structure, or at a site near one of the ends, or at a site at which addition of the sugar chain will not change the tertiary structure of said protein [greatly] sufficiently to cause said protein to incur a loss of activity.

14. (Twice Amended) A pharmaceutical composition containing the heparin-binding protein of any one of claims 1 [and] or 3-6 as an active ingredient.

16. (Twice Amended) A heparin binding protein comprising at least one covalently bonded sugar chain, wherein the at least one sugar chain is selected from the group consisting of a sulfated polysaccharide, a glycosaminoglycan, an O-linked sugar chain and combinations thereof, wherein the at least one sugar chain is covalently bonded through a peptide to which the sugar chain can be added, thereby increasing the residual activity of the heparin-binding peptide for the intended medical use by adding the at least one covalently bonded sugar chain.

18. (Amended) An improved heparin-binding protein which comprises [A] a heparin binding protein functionalized by covalently bonding thereto at least one sugar chain, wherein the at least one sugar chain is covalently bonded through a peptide to which the sugar chain can be added thereby increasing the residual activity of the heparin-binding peptide for the intended medical use, said at least one sugar chain selected from the group consisting of a sulfated polysaccharide, a glycosaminoglycan, an O-linked sugar chain and combinations thereof.

20. (Amended) [A] An improved heparin-binding protein comprising a heparin binding protein containing a peptide sequence to which at least one sugar chain is [can be] covalently bonded, wherein the at least one sugar chain is covalently bonded through [a] the peptide sequence to which the at least one sugar chain [can be] is added, thereby increasing the residual activity of the heparin-binding peptide for the intended medical use, said sugar chain selected from the group consisting of a sulfated polysaccharide, a glycosaminoglycan, an O-linked sugar chain and combinations thereof.